

File 155:MEDLINE(R) 1951-2006/Mar 01  
 (c) format only 2006 Dialog  
 File 55:Biosis Previews(R) 1993-2006/Feb W4  
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 File 34:SciSearch(R) Cited Ref Sci 1990-2006/Feb W4  
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 File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec  
 (c) 1998 Inst for Sci Info  
 File 340:CLAIMS(R)/US Patent 1950-06/Feb 28  
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**\*File 340: IPCR/8 classification codes now searchable in 2006 records.**  
 For important information about IC=index changes, see HELP NEWSIPCR.

Set	Items	Description
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? rmc20c001		
>>>Unrecognizable Command		
? s rmc20c001		
	S1	13 RMC20C001
? rd		

>>>Duplicate detection is not supported for File 340.

>>>Records from unsupported files will be retained in the RD set.  
 S2 5 RD (unique items)  
 ? t s2/3,k,ab/1-5

**2/3,K,AB/1 (Item 1 from file: 155)**  
 DIALOG(R)File 155:MEDLINE(R)  
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12773524 PMID: 10706127

**Relating genotype and phenotype in breast cancer: an analysis of the prognostic significance of amplification at eight different genes or loci and of p53 mutations.**

Cuny M; Kramar A; Courjal F; Johannsdottir V; Iacopetta B; Fontaine H; Grenier J; Culine S; Theillet C

Genome et Cancer UMR 5535 Centre National de la Recherche Scientifique, Centre de Recherche et de Lutte contre le Cancer Val d'Aurelle-Paul Lamarque, Montpellier, France.

Cancer research (UNITED STATES) Feb 15 2000, 60 (4) p1077-83, ISSN 0008-5472 Journal Code: 2984705R

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Breast cancer heterogeneity can be related directly to its variability at the genetic level. Thus, tumor genotyping could be a valuable approach to define breast tumor subtypes. It has been shown that it is possible to delineate subgroups of breast tumors according to specific sets of DNA amplifications. The aim of the present work was to study the prognostic significance of these DNA amplifications. We studied DNA amplification at eight genes or loci (AIB1, CCND1, EMS1, ERBB2, FGFR1, MDM2, MYC, and RMC20C001) as well as p53 mutations in a series of 640 breast cancer patients who had not received presurgical therapy and analyzed the correlations with survival DNA amplification was assessed by Southern blotting and was scored positive when exceeding three to five copies. Mutations in the p53 gene were searched by four-color fluorescent single.

strand conformational polymorphism, using an automated sequencer. Of the nine genetic alterations tested, four (CCND1, EMS1, FGFR1, and p53 mutations) showed a significant association with reduced disease-free (DFS) and/or overall survival (OVS) in the unselected set of patients by univariate test. Correlations for p53 were found only when selecting mutations in exons 5 or 7. Analysis of node-negative and -positive subgroups of patients showed that MDM2 amplification and p53 mutations bore prognostic significance in node-negative patients, whereas amplification of CCND1, EMS1, and FGFR1 correlated with poor outcome in node-positive patients. Multivariate analysis on an unselected set of patients retained significance for the amplification of EMS1, FGFR1, and MDM2 with DFS, of CCND1 with OVS, and of **RMC20C001** with both DFS and OVS. Interestingly, stratified analysis according to nodal status confirmed results obtained in the univariate tests: significance of MDM2 amplification and p53 mutations in node-negative and that of CCND1, EMS1, and FGFR1 in node-positive patients. We also observed an association between the number of genetic alterations observed in a tumor and poor prognosis. Patients with two or more amplified loci had a worsened outcome. Strongly correlating coamplifications such as CCND1 and FGFR1, as well as ERBB2 and MYC, were associated with a significant reduction of patient survival, thus indicating cooperative effects. Our data support the idea that genetic alterations in breast cancer are not only helpful for phenotyping purposes, but can also represent powerful prognostic indicators in the clinical practice.

... the amplification of EMS1, FGFR1, and MDM2 with DFS, of CCND1 with OVS, and of **RMC20C001** with both DFS and OVS. Interestingly, stratified analysis according to nodal status confirmed results obtained...

**2/3,K,AB/2 (Item 2 from file: 155)**

DIALOG(R) File 155:MEDLINE(R)

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12550547 PMID: 9865902

**In breast cancer, amplification of the steroid receptor coactivator gene AIB1 is correlated with estrogen and progesterone receptor positivity.**

Bautista S; Valles H; Walker R L; Anzick S; Zeillinger R; Meltzer P; Theillet C

Equipe Genome et Cancer UMR 5535 Centre National de la Recherche Scientifique, Centre de Recherche, Montpellier, France.

Clinical cancer research - an official journal of the American Association for Cancer Research (UNITED STATES) Dec 1998, 4 (12) p2925-9, ISSN 1078-0432 Journal Code: 9502500

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

The AIB1 gene was isolated upon microdissection of the homogeneously staining regions observed in breast cancer cell lines. It was subsequently shown to map at a region at 20q12 that is frequently amplified in breast tumors. In a screen of breast tumor cell lines, of all the genes mapping to the region, AIB1 appeared to be the most consistently amplified and overexpressed. AIB1 shares homology with the SRC-1 family of nuclear receptor coactivators. It was found to interact in a ligand-dependent manner with the estrogen receptor (ER) and to result in increased levels of estrogen-dependent transcription. These properties could be of important biological significance in breast and ovarian cancerigenesis, and we were,

therefore, interested in determining whether the amplification of the AIB1 gene was associated with a particular phenotype or subgroup in these tumors. We tested a population of 1157 breast and 122 ovarian tumors in which DNA amplification had been determined previously at 15 chromosomal locations. Amplification of the AIB1 gene was observed in 4.8% of breast cancers and 7.4% of ovarian cancers. In breast tumors, AIB1 was correlated with ER and progesterone receptor positivity, as well as with tumor size. Correlation was also observed with the amplification of MDM2 and FGFR1 genes, but interestingly, no correlation was found with the amplification of CCND1, which is known to be strongly associated with ER. Furthermore, analyzing at 20q12-q13 range, we show the existence of three amplification cores, represented by AIB3/AIB4, AIB1, and **RMC20C001**. AIB1 and CCND1 amplifications may, thus, represent two different subsets of ER-positive breast tumors.

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2/3,K,AB/3 (Item 3 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

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11736213 PMID: 9815944

**Amplification of chromosomal region 20q13 in invasive breast cancer:0 prognostic implications.**

Tanner M M; Tirkkonen M; Kallioniemi A; Holli K; Collins C; Kowbel D; Gray J W; Kallioniemi O P; Isola J

Laboratory of Cancer Genetics, Tampere University Hospital and Institute of Medical Technology, P.O. Box 2000, Fin-33521 Tampere, Finland.

Clinical cancer research - an official journal of the American Association for Cancer Research (UNITED STATES) Dec 1995, 1 (12) p1455-61, ISSN 1078-0432 Journal Code: 9502500

Contract/Grant No.: CA58207; CA; NCI

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Amplification of the chromosome 20q13 region was recently discovered in breast cancer by comparative genomic hybridization and subsequently further defined by fluorescence in situ hybridization with specific probes. The target gene of the amplification remains unknown. Here, fluorescence in situ hybridization with a cosmid probe for the minimal region of amplification ( **RMC20C001** ) was used to study 20q13 amplification in 132 primary breast carcinomas and 11 metastases. The size of the amplicon was studied with four flanking probes. Thirty-eight (29%) primary tumors and 3 (27%) metastases showed increased copy number of the **RMC20C001** probe (>1.5-fold relative to the p-arm control). Nine (6.8%) of the primary tumors were highly (>3-fold) amplified. Although the size and location of the amplified region varied from one tumor to another, only the **RMC20C001** probe was consistently amplified. 20q13 amplification was significantly associated with a high histological grade ( $P = 0.01$ ), DNA aneuploidy ( $P = 0.01$ ), and high S-phase fraction ( $P = 0.0085$ ). High-level amplification was also associated with short disease-free survival of patients with node-negative breast cancer ( $P = 0.002$ ). We conclude that high-level 20q13 amplification may be an indicator of poor clinical outcome in node-negative breast cancer and that this chromosomal region is likely to contain a gene

with an important role in breast cancer progression. A large definitive study is warranted to assess the independent prognostic value of 20q13 amplification.

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... Thirty-eight (29%) primary tumors and 3 (27%) metastases showed increased copy number of the **RMC20C001** probe (>1.5-fold relative to the p-arm control). Nine (6.8%) of the...

... size and location of the amplified region varied from one tumor to another, only the **RMC20C001** probe was consistently amplified. 20q13 amplification was significantly associated with a high histological grade (P...

**2/3,K,AB/4 (Item 4 from file: 155)**

DIALOG(R) File 155:MEDLINE(R)

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11572081 PMID: 8883970

**Amplifications of oncogene erbB-2 and chromosome 20q in breast cancer determined by differentially competitive polymerase chain reaction.**

Deng G; Yu M; Chen L C; Moore D; Kurisu W; Kallioniemi A; Waldman F M; Collins C; Smith H S

Geraldine Brush Cancer Research Institute at California Pacific Medical Center, San Francisco 94115, USA.

Breast cancer research and treatment (NETHERLANDS) 1996, 40 (3) p271-81, ISSN 0167-6806 Journal Code: 8111104

Contract/Grant No.: 1 P01 CA44768; CA; NCI; 1 P01 CA58207; CA; NCI

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

A new method of measuring gene copy number in small samples of DNA was used to measure amplification of the erbB-2 gene and of chromosome 20q in breast cancer. This method, termed 'differentially competitive polymerase chain reaction' (DC-PCR) combines the advantages of two other techniques for measuring amplification by PCR, namely differential PCR and competitive PCR. The DC-PCR methodology was evaluated for sensitivity and specificity by comparing amplification of erbB-2 measured by DC-PCR with that obtained by fluorescence in situ hybridization (FISH) for 42 cases or Southern blotting and/or slot blot analysis for 34 cases. There was over 90 percent concordance with both FISH and Southern blotting and/or slot blot analysis. DC-PCR was used to further characterize the newly described amplicon at chromosome 20q. By analyzing DNA from 10 breast cancer cell lines at 7 different loci, we identified a potential common region of amplification of approximately 5 centimorgans at chromosome 20q13 bordered by loci D20S52 and **RMC20C100-S1**. One hundred and seventeen cases of primary breast cancer were evaluated for amplification at these two loci. Amplification at one or more loci, defined as > 1.5 fold higher copy number than that of normal DNA, was found in 25 cases (21%). Sixteen cases were amplified at only one of the two probes (12 cases for **RMC20C001** -S1 and 4 cases for D20S52), suggesting that the target gene lies between the two markers or that there are two independent target genes within a small chromosome region.

... 21%). Sixteen cases were amplified at only one of the two probes (12

cases for **RMC20C001** -S1 and 4 cases for D20S52), suggesting that the target gene lies between the two...

2/3,K,AB/5 (Item 5 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

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11453370 PMID: 8758909

**Independent amplification and frequent co-amplification of three nonsyntenic regions on the long arm of chromosome 20 in human breast cancer.**

Tanner M M; Tirkkonen M; Kallioniemi A; Isola J; Kuukasjarvi T; Collins C ; Kowbel D; Guan X Y; Trent J; Gray J W; Meltzer P; Kallioniemi O P

Laboratory of Cancer Genetics, Institute of Medical Technology, Tampere University Hospital, Finland.

Cancer research (UNITED STATES) Aug 1 1996, 56 (15) p3441-5, ISSN 0008-5472 Journal Code: 2984705R

Contract/Grant No.: CA58207; CA; NCI

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

DNA amplification at 20q13.2 is common in breast cancer, correlates with poor prognosis, and may reflect location of an important oncogene. Recently, other regions along 20q were also found to undergo amplification. Here, amplification levels and patterns of co-amplification were analyzed by interphase fluorescence in situ hybridization at 14 loci along 20q in 146 uncultured breast carcinomas and 14 cell lines. Three regions were independently amplified in uncultured tumors: **RMC20C001** region at 20q13.2 (highly amplified in 9.6% of the cases), PTPN1 region 3 Mb proximal (6.2%), and AIB3 region at 20q11 (6.2%). Co-amplifications involving two or three of these regions were seen in 11 of the 19 highly amplified tumors. The results suggest that three distinct nonsyntenic regions along 20q may be important and that complex chromosomal rearrangements underlie their frequent co-amplification in breast cancer.

... uncultured breast carcinomas and 14 cell lines. Three regions were independently amplified in uncultured tumors: **RMC20C001** region at 20q13.2 (highly amplified in 9.6% of the cases), PTPN1 region 3...

? log off

02mar06 13:40:27 User231882 Session D1596.2

\$0.85 0.251 DialUnits File155

\$1.10 5 Type(s) in Format 4 (UDF)

\$1.10 5 Types

\$1.95 Estimated cost File155

\$0.57 0.096 DialUnits File55

\$0.57 Estimated cost File55

\$4.07 0.173 DialUnits File34

\$4.07 Estimated cost File34

\$0.45 0.019 DialUnits File434

\$0.45 Estimated cost File434

\$1.01 0.058 DialUnits File340

\$1.01 Estimated cost File340

OneSearch, 5 files, 0.597 DialUnits FileOS

\$0.53 TELNET

\$8.58 Estimated cost this search

\$8.61 Estimated total session cost 0.810 DialUnits

Logoff: level 05.10.03 D 13:40:27

You are now logged off

## Exhibit B

### GENBANK ENTRY AF312915



1: AF312915. Reports \_\_\_ Homo sapiens chro...[gi:11094030]

LOCUS AF312915 121143 bp DNA linear PRI 13-JUN-2001  
DEFINITION Homo sapiens chromosome 20 clones 97 and 127, complete sequence.

ACCESSION AF312915

VERSION AF312915.1 GI:11094030

KEYWORDS

SOURCE

Homo sapiens (human)

ORGANISM

Homo sapiens

Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini;  
Hominidae; Homo.

REFERENCE 1 (bases 1 to 121143)

AUTHORS

Collins,C., Volik,S., Kowbel,D., Ginzinger,D., Ylstra,B.,  
Cloutier,T., Hawkins,T., Predki,P., Martin,C., Wernick,M.,  
Kuo,W.L., Alberts,A. and Gray,J.W.

Comprehensive genome sequence analysis of a breast cancer amplicon  
Genome Res. 11 (6), 1034-1042 (2001)

TITLE

JOURNAL

PUBMED

REFERENCE 2 (bases 1 to 121143)

AUTHORS

Volik,S., Collins,C., Gray,J., Wernick,M., Kowbel,D., Stultz,K. and  
Martin,C.

Direct Submission

TITLE

JOURNAL

Submitted (10-OCT-2000) Cancer Genetics, UCSF Cancer Center, 2340  
Sutter St., Rm. S151, San Francisco, CA 94706, USA

Links

## Exhibit A

### Results of BLAST of SEQ ID NO:9

# BLASTN 2.2.12 [Aug-07-2005]

# Query:

# Database: nr

# Fields: query id, subject ids, % identity, alignment length, mismatches, gap opens, q. start, q. end, s. start, s. end, evalue, bit score

# 9399 hits found

1_10835 gi 11094030 gb AF312915.1 AF312915	100.00	7430	0	0	1	7430	107755	100326	0.0		
1.372e+04											
1_10835 gi 11094030 gb AF312915.1 AF312915	100.00	2909	0	0	7457	10365	100299	97391	0.0	5563	
1_10835 gi 11094030 gb AF312915.1 AF312915	88.16	245	19	8	7465	7704	63389	63628	3e-75	294	
1_10835 gi 11094030 gb AF312915.1 AF312915	83.66	257	32	10	7457	7708	44265	44516	1e-59	242	
1_10835 gi 11094030 gb AF312915.1 AF312915	86.79	212	20	8	7472	7679	77879	77672	2e-58	239	
1_10835 gi 11094030 gb AF312915.1 AF312915	86.11	216	25	5	7458	7671	51302	51514	7e-58	237	